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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
| 10/576,030 | 04/13/2006 | Masanori Yamaguchi | TOYA149001APC | 2081 |
| 20995 7590 09/09/2009 KNOBBE MARTENS OLSON & BEAR LLP 2040 MAIN STREET FOURTEENTH FLOOR IRVINE, CA 92614 | | | EXAMINER LAU, JONATHAN S | |
| | | | ART UNIT 1623 | PAPER NUMBER |
| | | | NOTIFICATION DATE 09/09/2009 | DELIVERY MODE ELECTRONIC |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
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ADVISORY ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 28 Aug 2009, in which claims 39 and 40 are canceled.

Applicant's Amendment AFTER FINAL limited to canceling claims 39 and 40, filed 28 Aug 2009, will be entered.

Finality of Office Action

Applicant's Remarks, filed 28 Aug 2009, have been fully considered and not found to be persuasive.

Applicant characterizes the amendment of March 6, 2009 as merely incorporating the limitations of claims 41 and 42, previously before the Examiner, into the base claim (claim 35). However, the amendment of March 6, 2009 amends the base claim 35 at line 2 to recite a "first step of precipitating a scyllo-inositol/boric acid complex..." This limitation is not found in the claims 41 and 42, reciting limitations of the fourth step. This amendment to base claim 35 at line 2 requires a manipulative difference in this first step of the method and changes the scope and breadth of the invention as claimed, and is newly presented in the amendment of March 6, 2009. Therefore, the amendment of March 6, 2009 is not limited to incorporating the limitations of claims 41 and 42 into the base claim (claim 35). Claims 36, 37, 39, 40 and 43 depend from claim 35 and incorporate all limitations therein, including changes to the scope and breadth of the invention as claimed.

The finality of the Office Action of June 23, 2009 is deemed proper, as new grounds of rejection were necessitated by amendment to the claims, and **maintained**.

Continuation of 5.

Rejections Withdrawn

Applicant's Amendment, filed 28 Aug 2009, with respect to Amended Claims 35-37, 39, 40 and 43 rejected under 35 U.S.C. 103(a) as being unpatentable over Merck (DE 3405663, published 22 Aug 1985, provided by Applicant on IDS mailed 26 May 2006) in view of Weissbach (Journal of Organic Chemistry, 1958, 23, p329-330, provided by Applicant on IDS mailed 26 May 2006) in view of Mopper (Analytical Biochemistry, 1978, 87, p162-168, of record) and in view of the Encyclopedia Britannica relied upon to show common knowledge in the art (entry for separation and purification, Encyclopedia Britannica Online, of record) has been fully considered and is persuasive with regard to claims 39 and 40, as claims 39 and 40 are canceled.

This rejection with regard to claims 39 and 40 has been **withdrawn**.

Continuation of 11. Applicant's Amendment AFTER FINAL limited to canceling claims 39 and 40, filed 28 Aug 2009, will be entered.

Amended Claims 35-37 and 43 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Merck (DE 3405663, published 22 Aug 1985, provided by Applicant on IDS mailed 26 May 2006) in view of Weissbach (Journal of Organic Chemistry, 1958, 23, p329-330, provided by Applicant on IDS mailed 26 May 2006) in view of Mopper

Art Unit: 1623

(Analytical Biochemistry, 1978, 87, p162-168, of record) and in view of the Encyclopedia Britannica relied upon to show common knowledge in the art (entry for separation and purification, Encyclopedia Britannica Online, of record).

Applicant's Remarks, filed 28 Aug 2009, have been fully considered and found not to be persuasive.

Applicant asserts that one of ordinary skill in the art would not expect that the scyllo-inositol/boric acid complex is formed during the procedure of Merck because the methanol is added to separate off the borate. However, the teaching of Weissbach, that scyllo-inositol is known to form a diborate complex with two borate moieties and that the reduction of scyllo-myo-inosose with sodium borohydride generates a mixture of scyllitol and myo-inositol from which the diborate of scyllitol precipitates, was known prior to the invention of Merck. Therefore one of ordinary skill in the art would expect the reduction of scyllo-myo-inosose with sodium borohydride as taught by Merck would produce the diborate of scyllitol, or the scyllo-inositol/boric acid complex.

Applicant notes that nowhere in Merck does Merck teach or suggest the formation of a scyllo-inositol/boric acid complex or its separation. However, the rejection is made over Merck in view of Weissbach in view of Mopper and in view of the Encyclopedia Britannica relied upon to show common knowledge in the art. Weissbach is relied upon to teach that the formation of a scyllo-inositol/boric acid complex as a precipitate resulting from reaction with sodium borohydride as taught by Merck was known to one of ordinary skill in the art and Mopper is relied upon to teach that separation of sugar-borate complexes are well known in the art.

Art Unit: 1623

Applicant notes that Merck discloses adding 200 mL of methanol to 20 mL of the acidic concentrate (lines 8-11 of translation of Merck provided by Applicants), or 10 times the volume of the acidic concentrate. Applicant states that this is quite different from the instantly claimed method, wherein methanol is added in a volume 0.3 to 5 times the volume of the acid solution or acid suspension (instant claim 35, lines 16-17). Applicant asserts that the purpose of adding methanol in Merck is azeotropy, and is therefore different from the purpose of adding methanol to precipitate scyllo-inositol in the fourth step of the claimed invention. However, the function of azeotropy is to remove the reaction solvent from a product, and this achieves the same purpose as precipitation to remove a product from the reaction solvent. Therefore it would have been obvious to perform routine optimization of the amount of solvent used for the same purpose of separating a product from the reaction solvent.

Applicant notes that neither Weissbach nor Merck teach the precipitation of a scyllo-inositol/boric acid complex by adding a boric acid and metal salt and Weissbach fails to teach precipitation with methanol or ethanol. However, Mopper is relied upon to teach that the conditions in which sugars react with borate to form a complex in solution by optimizing both pH and sample salinity. Salinity within this context is implicitly NaCl, which in solution with boric acid necessarily forms borax, or sodium borate. Both NaCl and borax are recited within instant claim 35. Weissbach is silent as to the solvent of the reaction mixture from which the reduction with sodium borohydride forms a precipitate (Weissbach page 329, right column, paragraph 2), however Merck teaches

Art Unit: 1623

that the reaction conditions for this reduction are sodium borohydride in methanol (Merck machine translation page 2, paragraph 6).

Applicant notes that ion exchange chromatography is a separations method based on the equilibrium of the reaction of a compound with an ion exchangeable functional group of the column while precipitation is a separations method based on the liquid-solid equilibrium, and that therefore one of ordinary skill in the art would not interpret them as equivalent methods of separation. However, ion exchange chromatography is a separations method based on the equilibrium of the compound dissolved in the liquid phase and the compound associated with the solid phase in the form of the column material, whereas precipitation is a separations method based on the equilibrium of the compound dissolved in the liquid phase and the compound associated with the solid phase in the form of the precipitate. Within the specific context of separations methods based on liquid-solid phase equilibria, it is well within the level of one of ordinary skill in the art to substitute one well known separations method for another, and therefore *prima facie* obvious to one of ordinary skill in the art.

Applicant asserts that Mopper does not teach the limitations of the instant invention. However, Mopper is relied upon to teach that the conditions in which sugars react with borate to form a complex in solution, at pH 8.63, and that it is recognized by one of ordinary skill in the art at the time of the invention to optimize both pH and sample salinity. Salinity within this context is implicitly NaCl, which in solution with boric acid at pH 8.63 necessarily forms borax, or sodium borate. Both NaCl and borax are encompassed within the scope of the metal salt recited instant claim 35.

Art Unit: 1623

Applicant notes that Mopper teaches that sugars generally react weakly with borate to form a complex in solution. However Weissbach teaches the stereochemistry specific to scyllo-inositol results in formation of the diborate sodium salt that precipitates from solution. Applicant notes that Mopper is drawn to separations by column chromatography, however Mopper is also drawn to the broader field of formation of sugar-borate complexes for the purpose of separations.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The rejection is made over Merck in view of Weissbach in view of Mopper and in view of the Encyclopedia Britannica relied upon to show common knowledge in the art, and it is acknowledged in the Office Action of June 23, 2009 that Merck does not individually disclose the invention as claimed. As discussed herein, the references individually do not render obvious the invention as claimed. However, the invention as claimed would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention over the combined teachings of the prior art as detailed in the Office Action of June 23, 2009 and discussed herein.

This rejection of amended claims 35-37 and 43 is **maintained**.

/Shaojia Anna Jiang/

Supervisory Patent Examiner, Art Unit 1623

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| <p align="center">Advisory Action Before the Filing of an Appeal Brief</p> | Application No. 10/576,030 | Applicant(s) YAMAGUCHI ET AL. | |
| | Examiner Jonathan S. Lau | Art Unit 1623 | |

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 21 August 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
 b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
 Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
 (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
 (b) ☐ They raise the issue of new matter (see NOTE below);
 (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
 5. ☒ Applicant's reply has overcome the following rejection(s): see continuation sheet.
 6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
 7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
 The status of the claim(s) is (or will be) as follows:
 Claim(s) allowed: none.
 Claim(s) objected to: none.
 Claim(s) rejected: 35-37 and 43.
 Claim(s) withdrawn from consideration: none.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see continuation sheet.
 12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
 13. ☐ Other: _____

/Shaojia Anna Jiang/
 Supervisory Patent Examiner, Art Unit 1623